

Pending claims:

1-22. **Cancelled**

23. **(Currently amended)** A transgenic non-human animal having a transgene integrated into the genome of the non-human animal and also having a *tet* operator-linked gene in the genome of the non-human animal, wherein:

the transgene comprises a transcriptional regulatory element functional in cells of the non-human animal operatively linked to a polynucleotide sequence encoding a fusion protein which activates transcription of said *tet* operator linked gene,

the fusion protein comprises a first polypeptide which is a Tet repressor operatively linked to a second polypeptide which directly or indirectly activates transcription in eukaryotic cells,

said *tet* operator-linked gene is expressed at detectable levels ~~confers a detectable and functional phenotype on the non-human animal when expressed~~ in cells of the non-human animal,

said transgene is expressed in cells of the non-human animal at a level sufficient to produce amounts of said fusion protein that are sufficient to activate transcription of the *tet* operator-linked gene; and

in the absence of tetracycline or a tetracycline analogue in the non-human animal, said fusion protein binds to the *tet* operator-linked gene and activates transcription of the *tet* operator linked gene such that the *tet* operator-linked gene is expressed at a detectable level ~~in sufficient to confer the detectable and functional phenotype on the non-human animal~~, wherein the level of expression of the *tet* operator-linked gene can be downmodulated by administering tetracycline or a tetracycline analogue to the non-human animal.

24. **(Currently amended)** A transgenic non-human animal having a transgene integrated into the genome of the non-human animal, wherein:

the transgene comprises a transcriptional regulatory element functional in cells of the non-human animal operatively linked to a polynucleotide sequence encoding a fusion protein which activates transcription of a *tet* operator linked gene at a detectable level,

the fusion protein comprising a first polypeptide which is a Tet repressor, operatively linked to a second polypeptide which directly or indirectly activates transcription in eukaryotic cells, and

said transgene fusion protein is expressed in cells of the non-human animal.

25. **(Previously presented)** The non-human animal of claim 23, wherein the second polypeptide of the fusion protein comprises a transcription activation domain of herpes simplex virion protein 16.

26. **(Previously presented)** The non-human animal of claim 24, wherein the second polypeptide of the fusion protein comprises a transcription activation domain of herpes simplex virion protein 16.

27-30. **Cancelled**

31. **(Previously presented)** The non-human animal of claim 23, wherein the *tet* operator-linked gene is a second transgene comprising a gene of interest operably linked to at least one *tet* operator sequence.

32. **(Previously presented)** The non-human animal of claim 24, wherein the *tet* operator-linked gene is an endogenous gene that has been operatively linked to at least one *tet* operator sequence.

33. **(Previously presented)** The non-human animal of claim 23, which is selected from the group consisting of: a mouse, a cow, a sheep, a goat, and a pig.

34. **(Previously presented)** The non-human animal of claim 24, which is selected from the group consisting of: a mouse, a cow, a sheep, a goat, and a pig.

35. **(Currently amended)** A transgenic non-human animal selected from the group consisting of a mouse, a cow, a sheep, a goat, and a pig, having a transgene integrated into the genome of the non-human animal and also having a *tet* operator-linked gene in the genome of the non-human animal, wherein:

the transgene comprises a transcriptional regulatory element functional in cells of the non-human animal operatively linked to a polynucleotide sequence encoding a fusion protein which activates transcription of said *tet* operator linked gene,

the fusion protein comprises a first polypeptide which Tet repressor operatively linked to a second polypeptide which directly or indirectly activates transcription in eukaryotic cells,

said *tet* operator-linked gene is expressed at detectable levels ~~confers a detectable and functional phenotype on the organism when expressed~~ in cells of the non-human animal,

said transgene is expressed in cells of the non-human animal at a level sufficient to produce amounts of said fusion protein that are sufficient to activate transcription of the *tet* operator-linked gene; and

in the absence of tetracycline or a tetracycline analogue in the non-human animal, said fusion protein binds to the *tet* operator-linked gene and activates transcription of the *tet* operator linked gene such that the *tet* operator-linked gene is expressed at a detectable level ~~in sufficient to confer the detectable and functional phenotype on the non-human animal~~, wherein the level of expression of the *tet* operator-linked gene can be downmodulated by administering tetracycline or a tetracycline analogue to the non-human animal.

36. **(Currently amended)** A transgenic non-human animal selected from the group consisting of a mouse, a cow, a sheep, a goat, and a pig having a transgene integrated into the genome of the non-human animal, wherein:

the transgene comprises a transcriptional regulatory element functional in cells of the non-human animal operatively linked to a polynucleotide sequence encoding a fusion protein which activates transcription of a *tet* operator linked gene at a detectable level,

the fusion protein comprising a first polypeptide which is a Tet repressor, operatively linked to a second polypeptide which directly or indirectly activates transcription in eukaryotic cells, and

said transgene ~~fusion protein~~ is expressed in cells of the non-human animal.

37. **(Previously presented)** The non-human animal of claim 35, wherein the second polypeptide of the fusion protein comprises a transcription activation domain of herpes simplex virion protein 16.

38. **(Previously presented)** The non-human animal of claim 36, wherein the second polypeptide of the fusion protein comprises a transcription activation domain of herpes simplex virion protein 16.

39. **(Previously presented)** The non-human animal of claim 35, wherein the *tet* operator-linked gene is a second transgene comprising a gene of interest operably linked to at least one *tet* operator sequence.

40. **(Previously presented)** The non-human animal of claim 36, wherein the *tet* operator-linked gene is an endogenous gene that has been operatively linked to at least one *tet* operator sequence.